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| EXAMINER | |
|---|---|
| SISSON, BRADLEY L | |

| ART UNIT | PAPER NUMBER |
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| 1634 | |

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/582,820 | HE ET AL. | |
| | Examiner | Art Unit | |
| | Bradley L. Sisson | 1634 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *23 December 2009 and 28 May 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-7* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *28 May 2010* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

### *Priority*

1. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

### *Drawings*

2. The drawings were received on 28 May 2010. These drawings are acceptable.

### *Claim Rejections - 35 USC § 112*

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1-7 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

5. Claim 1 is the sole independent claim pending. For convenience, claim 1 is reproduced below.

1. (currently amended) A method for detecting a target nucleic acid comprising:

(a) providing first and second target-specific nucleic acids, wherein the first and second target-specific nucleic acids each comprise sequences complementary to the target nucleic acid; wherein the first target specific nucleic acid is bound to a first affinity tag and the second target-specific nucleic acid is bound to a second affinity tag, wherein the first affinity tag is capable of binding to a molecular motor, wherein the molecular motor comprises a biological or synthetic molecule capable of induced translational or rotational movements that are capable of detection, and wherein the second affinity tag is capable of binding to a detection probe;

(b) contacting the first and second target-specific nucleic acids to a sample under conditions whereby the first and second target-specific nucleic acids will hybridize to the target nucleic acid if the target nucleic acid is present in the sample, wherein upon hybridization to the target nucleic acid the first and second target-specific nucleic acids are directly adjacent to each other;

(c) ligating the first and second target-specific nucleic acids together;

(d) binding the molecular motor to the first affinity tag and the detection probe to the second affinity tag;

(e) inducing movement of the molecular motor; and

(f) detecting movement of the molecular motor through the detection probe, wherein the movement of the molecular motor serves to detect the target nucleic acid in the sample.

6. .For purposes of examination, the method of claim 1 has been construed as not requiring either the first and second target-specific nucleic acids be immobilized, directly or indirectly to any solid support. Also, said claim has been construed as not requiring either the affinity tag or the target nucleic acid be bound, directly or indirectly, to any solid support. Accordingly, the reactants have been construed as being freely moving about in solution.

7. Claim 1 has also been construed as not requiring any direct detection of any molecular motor, but rather, as requiring detection of the probe (step (f)) and that by detection of the probe, one is to infer that the molecular motor is present.

8. The claim has also been construed as not requiring the removal of any unincorporated reactants. Accordingly, the total amount of probe present is kept constant.

9. The method of claim 1 does not specify just what property(ies) of the probe is/are being detected. Accordingly, the claim has been construed as requiring nothing more than detection of the probe's presence. It stands to reason, therefore, that with the total amount of probe being present throughout the assay, that one of skill in the art would be detecting probe whether or not any target was present, and that this detection of probe would then, erroneously, be construed as indicating some movement of the (unbound) molecular motor as being present, and thusly, and erroneously, reach the conclusion that the target nucleic acid was also present.

10. For purposes of examination, claim 1 has also been construed as requiring ligation of first and second target-specific nucleic acids together irrespective of their having hybridized, or not hybridized, to the target nucleic acid. Note: While claim 1 does specify that the first and second target nucleic acids will hybridize to target only if the target is present, no requirement of a precondition of hybridization to target is required for the step ligating first and second target-specific nucleic acids.

11. Acknowledgement is made of applicant having amended claim 1 to now recite, "The molecular motor comprises a biological or synthetic molecule capable of induced translational or rotational movements that are capable of detection." It is noted, however,

that the translational or rotational movements are not specified as being that which is being detected. Further, with all members of the reaction in solution, it stands to reason that said members of the reaction, including the probe, would be freely moving about, be it Brownian movement and/or response to thermal currents in the solution and therein exhibiting some form of translational or rotational movement. Indeed, even if the target nucleic acid were immobilized on one end, the unbound portion would still be free to move about- irrespective of the molecular motor and probe. This is in contrast to applicant's assertions at parts (a) and (b) of page 11 of the response of 23 December 2009.

12. For purposes of examination, the claimed method has been construed as encompassing the simultaneous detection of multiple target nucleic acids. The claims have not been construed as requiring the use of different molecular motors and/or different probes. Accordingly, it would not be possible to determine which, if any, of an assortment of different target nucleic acid(s) is/are present in any given sample.

13. Applicant, at page 11, bridging to page 12, of the response of 23 December 2009 directs attention to page 15 of the disclosure as teaching the use of different nanorods with different affinity tags. This argument has been considered and has not been found persuasive as applicant is arguing limitations not present in the claims. It is noted with particularity that narrowing limitations found in the specification cannot be inferred in the claims where the elements not set forth in the claims are linchpin of patentability. *In re Philips Industries v. State Stove & Mfg. Co, Inc.*, 186 USPQ 458 (CA6 1975). While the claims are to be interpreted in light of the specification, it does not follow that limitations from the specification may be read into the claims. On the contrary, claims must be

interpreted as broadly as their terms reasonably allow. See *Ex parte Oetiker*, 23 USPQ2d 1641 (BPAI, 1992).

14. For purposes of examination, claim 1 has been construed as requiring the use of a first and second "target specific nucleic acid." However, the aspect that the first and second target-specific nucleic acids be "specific" for only the target(s) of interest has not been read into the claims. Rather, the claims have been construed as encompassing a nucleic acids that are complementary to a region that is found within the target- and may also be found in some other nucleic acids as well. For example, the first and second target-specific nucleic acids may be 100% complementary to a region within the target, e.g., the six nucleotides that constitute an *EcoRI* restriction endonuclease recognition site, or the terminal poly-A region of virtually all mammalian genes. Cleary, with the probes being 100% complementary to these regions that are arguably "specific," but may also hybridize to the same sequence when present. A review of applicant's argument at page 9, bridging to page 10, of the response of 23 December 2009 seemingly implies that to be specific it must also be unique. Such a limitation has not been read into the claims.

15. Claims 1-7 are not enabled by the specification as the specification does not disclose a representative number of species of first and second target-specific nucleic acid that hybridize "directly adjacent to each other." In support of this position, it is noted that the clamed method encompasses the detection of any target nucleic acid, be it from any animal, plant, bacteria, virus, artificial chromosome, etc. The specification, however, discloses but 4 sequences, which are all described in the Sequence Listing as being "Synthetic Oligonucleotide" and range in length of 25-42 nucleotides in length.

16. Applicant, at page 12 of the response of 23 December 2009 states:

> The Office asserts that the specification "fails disclose first and second target-specific nucleic acids that hybridize 'directly adjacent' to one another on any and all manner of target nucleic acids..." Applicants note that this statement clearly indicates a misunderstanding of the claimed invention. There is no requirement that the first and second target-specific nucleic acids hybridize directly adjacent to one another on all target nucleic acids. In fact, the target-specific nucleic acids are by virtue of their complementarity (as well as the first and second target- specific nucleic acids binding to the target so that they are directly adjacent) to only the target nucleic acid being analyzed. In other words, the target-specific nucleic acids will be different for each target (as implied by the name "target-specific"). Thus, it will be clear that Applicants have no obligation to teach "first and second target-specific nucleic acids that hybridize directly adjacent to one another on all target nucleic acids", as this is not part of the present invention. (Emphasis added.)

The above argument has been considered and has not been found persuasive. It is noted with particularity that claim 1, the only independent claim, explicitly states, "wherein upon hybridization to the target nucleic acid the first and second target specific nucleic acids **are directly adjacent** to each other" (emphasis added). Further, the specification, at page 4, first full paragraph, states:

> As used herein the term "directly adjacent" means juxtaposed 5' phosphate and 3' hydroxyl termini of two adjacent target-specific nucleic acids hybridized to the complementary target nucleic acid~ which can be ligated together by the action of a nucleic acid ligase.

In view of this explicit language as to how the expression is to be construed, claim 1, and claims that depend therefrom, are deemed to be limited to those first and second target-specific nucleic acids that do in fact hybridize immediately adjacent to one another such that a ligase will join the tow together.

17. Again, applicant has not provided a representative number of those first and second target-specific nucleic acids that would enable the generic method being claimed.

18. Assuming *arguendo* that the claims were amended so to recite that the first and second target-specific nucleic acids are not immediately adjacent to one another, the

claimed method is still deemed to be non-enabled as the method does not require that the gap(s) between the two target-specific nucleic acids be filled in so that ligation could occur.

19. Claims 2-7, which depend from claim 1, fail to overcome these issues and are similarly rejected.

20. For the above reasons, and in the absence of convincing evidence to the contrary, claims 1-7 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement.

21. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

22. Claims 1-7 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

23. Claim 1 is indefinite with respect to what constitutes a "molecular motor." While applicant has amended claim 1 so to recite that "the molecular motor comprises a biological or synthetic molecule capable of induced translational or rotational movements that are capable of detection." Such a limitation seemingly encompasses any and all manner of molecules as any form of matter can be forced to move either translaitonally or rotationally. With the claim specifying that the molecule can be "synthetic," such does not define the population of molecules such that one would be readily able to determine which compounds is/are encompassed by the claims. Claims 2-7, which depend from

claim 1, fail to overcome this issue and are similarly rejected. While claim 3 does specify that the "molecular motor comprises F1-ATPase," such has not been construed as meaning that F1-ATPase is a molecular motor, but rather, that the molecular motor "comprises" this enzyme. By way of analogy, a set of golf clubs in the truck of a car does not make a car, yet the car comprises them. Furthermore, by simply looking at the set of golf clubs one would not have any meaningful description of just what constitutes the metes and bounds of car- which in and of its self is recognized as being capable of both detectable rotational and translational movement.

24. Claim 1 remains indefinite with respect tot what constitutes a "detection probe." At page 5 of the response of 23 December 2009, argument is presented as to what one of skill in the art would have construed the term to mean. This argument has been fully considered and has not been found persuasive. Attention is directed to MPEP 2145.

> Attorney argument is not evidence unless it is an admission, in which case, an examiner may use the admission in making a rejection. See MPEP § 2129 and § 2144.03 for a discussion of admissions as prior art.
> The arguments of counsel cannot take the place of evidence in the record. *In re Schulze*, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965); *In re Geisler*, 116 F.3d 1465,
> 43 USPQ2d 1362 (Fed. Cir. 1997) ("An assertion of what seems to follow from common experience is just attorney argument and not the kind of factual evidence that is required to rebut a prima facie case of obviousness."). See MPEP § 716.01(c) for examples of attorney statements which are not evidence and which must be supported by an appropriate affidavit or declaration.

25. Claims 5-7 are indefinite with respect to what constitutes the metes and bounds of "metal nanorod." Acknowledgement is made of where applicant, at page 5 of the response of 23 December 2009, directs attention to pages 14, ll. 14-18; page 15, ll. 29-32; and page 19, line 15, bridging to page 20, line 28, as providing a definition of the term.

26. The above argument, and sections of specification, have been considered and have not been found persuasive toward the withdrawal of the rejection. While the specification has provided examples of what a metal nanorod could be, there is no language that sets the metes and bounds of what the term/expression is to encompass.

27. Acknowledgement is also made of applicant's argument that one of skill in the art would understand jut what the term encompasses. However, this argument is void of any factual underpinning, including, but not limited to, any showing of just what the alleged art-recognized metes and bounds of the term are

***Conclusion***

28. Objections and/or rejections which appeared in the prior Office action and which have not been repeated hereinabove have been withdrawn.

29. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

30. A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

31. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bradley L. Sisson whose telephone number is (571) 272-0751. The examiner can normally be reached on 6:30 a.m. to 5 p.m., Monday through Thursday.

32. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dave T. Nguyen can be reached on (571) 272-0731. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

33. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Bradley L. Sisson/
Primary Examiner, Art Unit 1634